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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/813,747	03/29/2004	Stan Gronthos	75990-B/JPW/BJA	7277

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EXAMINER	
BELYAVSKYI, MICHAIL A	
ART UNIT	**PAPER NUMBER**
1644	
MAIL DATE	**DELIVERY MODE**
10/19/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/813,747	GRONTHOS ET AL.	
	Examiner	Art Unit	
	Michail A. Belyavskyi	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 July 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *79-90* is/are pending in the application.

4a) Of the above claim(s) *82,83 and 86-89* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *79-81,84,85 and 90* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *03/29/04* is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment, filed 07/05/07 is acknowledged.

2. Claims 79-90 are pending.

3. Applicant's election with traverse of Group I, claims 79-81,84,85 and 90 in the reply filed on 07/05/07 is acknowledged. Applicant traverse the Restriction Requirement on the grounds that the inventions must be both independent and distinct and an undue search burden on the examiner. However, MPEP 803 states that the Inventions be either independent or distinct and a burden on the Examiner if restriction is required.

Regarding applicant's comments about undue burden, the MPEP 803 (August 2001) states that "For purposes of the initial requirement, a serious burden on the examiner may be prima facie shown if the examiner shows by appropriate explanation either separate classification separate status in the art, or a different field of search". The Restriction Requirement enunciated in the previous Office Action meets this criteria, indicates that inventions recognized divergent subject matter and that a different field of search would be required based upon the structurally distinct products recited and the various methods of use comprising distinct method steps. Moreover, a prior art search also requires a literature search. All the above establishes that serious burden is placed on the examiner by the examination of more than one Group. The Inventions are distinct for reasons elaborated in the previous Office Action and above.

The requirement is still deemed proper and is therefore made FINAL.

Claims 82,83, 86-89 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to nonelected inventions.

Claims 79-81, 84, 85 and 90 read on a method of generating a tissue, wherein a tissue is a mesenchymal tissue in a subject, comprising administering to a subject a population of STRO-1 ^{bright} *cell are under consideration in the instant application.*

4. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 79-81, 84, 85 and 90 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a New Matter rejection.**

" a method of generating a tissue, wherein a tissue is a mesenchymal tissue in a subject, comprising administering to a subject a population of STRO-1 ^{bright} cell" claimed in claims 79-81, 84, 85 and 90 represent(s) a departure from the specification and the claims as originally filed and applicant has not pointed out where the support come(s) from.

The specification and the claims as originally field only support for a method for enriching for a MPC and for subpopulation of STRO-1 ^{bright} cell in particular.

7. Claims 79-81, 84, 85 and 90 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification disclosure does not enable one skilled in the art to practice the invention without an undue amount of experimentation.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the limited working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention.

The specification only discloses detailed *in vitro* method for isolation and purification of SRTO-1 ^{bright} BM MPC (see examples 1 in particular). The Specification further disclosed *in vitro* studies of possible chondrogenic potential of said SRTO-1 ^{bright} BM MPC. However, the instant Specification explicitly stated that within SRTO-1 ^{bright} /VCAM-1 ^{brigh} BM fraction there are several additional sub-fractions that might have different developmental potential (see page 32 in particular). The specification does not adequately teach how to effectively generate any mesenchymal tissue in any subject, including humans by administering a population of STRO-1 ^{bright} cells. Moreover, no animals models were used to study the effectively of generating any mesenchymal tissue in any subject, including humans by administering a population of STRO-1 ^{bright} cells. Since there is no animal model studies and data in the specification to show the effectively of generating any mesenchymal tissue in any subject, including humans by administering a population of STRO-1 ^{bright} cells. it is unpredictable how to correlate *in vitro* results with *in vivo* use . The specification does not teach how to extrapolate data obtained from *in vitro* studies to the development of effective *in vivo* mammalian therapeutic treatment, commensurate in scope with the claimed invention.

Hansson et al ., (Stem Cells, 2007, V.25, pages 1507-1510) teach that the data obtained on isolated stem cells *in vitro* has a limited , if any, correlation , for *in vivo* studies using said cells. The act of placing the stem cells into culture medium implies modifications which alters their biological properties compared to cells *in vivo*. Isolation and maintaining stem cells in vitro reqires a stringent selection for proliferation and adaptation to growth in tissue culture and thus **produces cells that have no counterpart in the normal animal** (emphases added). Thus, isolated stem cells *in vitro* can be viewed as something other than the stem cell existing as part of a human body (see entire document, Abstract and page 1508 in particular). does not well correlate In addition, Cochlovius et al (Modern Drug Discovery, 2003, pages 33-38) teach that in contrast to in vitro models, and partly animal-human xenograft systems, tissue cells in vivo seems to express molecules for defense against cellular immune systems as well as against complement. Although these defense mechanisms are still poorly understood, they provide some hints as to why many potential therapeutics perform marvelously *in vitro* but a fairly high portion of them still fail *in vivo*. Thus, in the absence of working examples or detailed guidance in the specification, the intended uses of STRO-1 ^{bright} cells in the method of generating any mesenchymal tissue in any subject, including human are fraught with uncertainties.

Although, the specification describes several *in vitro* data, there is no correlation on this record between the said results and a claimed method of generating any mesenchymal tissue in any subject by administering STRO-1 ^{bright} cells in currently available form for humans or animals. It is not enough to rely on in vitro studies where, as here, a person having ordinary skill in the art has no basis for perceiving those studies as constituting recognized screening procedures with clear relevance to efficacy in humans or animals (emphasis added). Ex parte Maas, 9 USPQ2d 1746.

Thus, Applicant has not provided sufficient guidance to enable one skill in the art to use claimed method of generating any mesenchymal tissue in any subject by administering STRO-1 ^{bright} cells in manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement. *In re Fisher*, 166 USPQ 18(CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

In view of the quantity of experimentation necessary, the unpredictability of the art, the lack of sufficient guidance in the specification, the limited working examples, and the limited amount of direction provided given the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

8. No claim is allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michail Belyavskyi whose telephone number is 571/272-0840. The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571/272-0841.

The fax number for the organization where this application or proceeding is assigned is 571/273-8300

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MICHAIL BELYAVSKYI, PH.D.
PATENT EXAMINER

10/10/07